REMARKS

Claims 42 and 61-64 were withdrawn as drawn to a non-elected invention and have been cancelled without prejudice or disclaimer. Claims 65-67 are pending. Claim 67 and 68 are new. Support for the new claims can be found on pages 8 and 37 of the Applicants' specification and elsewhere.

Claim 65 is objected to for having the informality of having a dash rather than a superscripted symbol of the negative charge in lines 7, 8, and 14. Claim 65 has been amended accordingly. Withdrawal of the objection is respectfully requested.

Claims 65 and 66 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the enablement requirement. Specifically, the rejection alleges that the claims are drawn to treating factors involved in fibrosis with a genus of polymers, but are enabled only for RGTA 1112 and 1113. The rejection alleges that undue experimentation is required for one skilled in the art to determine other suitable AXYZ polymers because such experimentation would constitute a "trial and error process."

The Applicants respectfully submit that the test of enablement is whether one reasonably skilled in the art could make or use the subject matter from the disclosures in the specification coupled with information known in the art without undue experimentation. The test is not whether any experimentation is necessary, but whether any necessary experimentation is undue. The Applicants respectfully submit that the Applicants' specification provides sufficient guidance and information to allow one skilled in the art to make and use AXYZ polymers for the treatment of fibroses. Any experimentation necessary to make and use the claimed subject matter is not undue because guidance is provided and the art routinely engages in such experimentation.

The Applicants respectfully submit that one of skill in the art is sufficiently enabled to make the claimed subject matter because the specification describes a process for synthesizing AXYZ polymers. Only routine procedures are required to synthesize particular polymers after consulting the Applicants' specification. Furthermore, the specification goes beyond the requirements of §112 and discloses both suitable and unsuitable biomolecules in the context of A, X, Y, and Z groups. Therefore, the Applicants respectfully submit that the specification provides sufficient guidance for one skilled in the art to make the claimed AXYZ polymers.

The Applicants respectfully submit that contrary to the assertions on Page 4 of the Official Action, the claims do not recite an "infinite number of polymers." For example, the specification and rejected Claims 65 and 66 recite that Z may be a fatty acid, amino acid, fatty alcohol, ceramide or derivatives thereof, and nucleotide addressing sequences. The specification also teaches that substances that have carcinogenic, mutagenic, or toxic properties, such as benzylamide, are excluded from use as a Z group (See page 9, line 23 of the Applicants' specification). Therefore, the claims do not encompass an infinite number of polymers. The Applicants' specification limits the possibilities to selected categories and even cautions against certain possibilities. Thus, one skilled in the art is enabled to make the polymers claimed in Claims 65 and 66. The fact that one skilled in the art might need to do some experimentation, even a fair amount of experimentation, does not mean that such experimentation is undue so long as it is routine.

Moreover, the Applicant's respectfully submit that the specification provides guidance with respect to assessing functional AXYZ polymers and use of the polymers to treat fibroses. Indeed, Examples 12 and 13 of the Applicants' specification set forth *in vitro* experimental protocols for assessing whether compounds possess anti-fibrotic activity. The specification teaches that anti-fibrotic effects can be evaluated by means of the quantity and quality of the secreted collagens. For example, the applicants describe the *in vitro* model of human intestinal smooth muscle cells cultured in DMEM medium treated with various quantities of RGTA. The cells can be treated with ^{60}cobalt irradiation and the collagen can be isolated and quantified on an SDS-polyacrylamide gel. Anti-fibrotic activity can be correlated with the amount of secreted collagen by determining if the amount of collagen III secretion in irradiated cells treated with the polymer is consistent with the amount secreted from non-irradiated control cells or irradiated cells without polymer treatment.

Fig. 26 of the Applicants' specification shows the results of the experimental protocol and confirms that two of the claimed AXYZ polymers, RGTA 1112 and 1113, possess anti-fibrotic activity. Therefore, Fig. 26 demonstrates successful reduction to practice of the experimental protocols for two representative polymers described in the specification. The protocols are repeatable with other polymers in a routine matter. Contrary to the rejection, Fig. 26 indicates that the specification provides sufficient guidance to support enablement of each claimed AXYZ polymer, and is not limited to assessing RGTA 1112 and 1113.

Indeed, the post-filing studies discussed in the attached Declaration present data that confirms the anti-fibrotic activity of AXYZ polymers. For example, an unpublished abstract of a study performed by Professor J. M. Denoix at the French National Veterinary School investigated the response of equine tendonitis to OTR4131, an AXYZ polymer in which A is glucose, X is carboxymethyl, Y is sulfate, and Z is acetate. This study demonstrated that horses diagnosed with tendonitis did not develop fibrotic tissue after an intratendon injection of OTR4131. Indeed, the tissue density of the diseased tendons regenerated and the organization of the tissue appeared normal. Similarly, OTR4131 and OTR4336 treatment of the cornea resulted in recovered transparency. Topical application of OTR4336 also prevented the formation of hypertrophic scars at the site of skin ulcers.

Additionally, in an unpublished study by Mangoni et al. and an abstract published in the 12th European Cancer Conference Organization, the authors reported on the response of radiation-induced mucositis, a form of fibrosis, to the administration of OTR4131. The authors found that labial mucosas treated with OTR4131 and isolated from mice 9 days after irradiation had reduced tissue thickness, collagen secretion, and leukocyte infiltration compared to untreated samples. Tissue samples treated with OTR4131 and collected 19 days after irradiation were indistinguishable from non-irradiated samples. The authors of Mangoni et al. concluded that anti-inflammatory properties, as indicated by reduced leukocyte infiltration in treated samples, are likely responsible for the protection against mucositic fibrosis.

Taken together, the work of Denoix and Mangoni et al. confirm that AXYZ polymers have anti-fibrotic effects when Z is acetate. Therefore, contrary to the assertions on page 4 of the Official Action, the rejected claims are enabled for polymers in addition to those shown in Fig. 26 of the Applicant's specification.

In light of the guidance provided in the Applicants' specification, the Applicants respectfully submit that the specification fully enables one skilled in the art to make and use AXYZ polymers without undue experimentation. Indeed, post-filing publications confirm use of particular polymers to treat and prevent fibrosis. Although a certain degree of routine experimentation may be required, the amount of experimentation is not undue because the Applicants' specification provides sufficient guidance and direction in making and identifying useful polymers. Indeed, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to

the direction in which the experimentation should proceed. Accordingly, reconsideration and withdrawal of the enablement rejection is respectfully requested.

Claims 65 and 66 are also rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. The rejection states that the recitation of what Z represents in lines 9-12 of Claim 65 comprises new matter because Page 22 of the Applicants' specification allegedly limits Z to –CO-OCH3-CH(CH2-CH3)CH3 when the A, X, and Y components are as indicated in the example on page 22.

The Applicants respectfully submit that the polymer described on Page 22 is a non-limiting example of an AXYZ polymer. Indeed, the paragraph in which this polymer is describes begins with the phrase, "in this example." Furthermore, beginning on Page 8 of the specification, the Applicants describe several different Z groups and do not suggest that a selection of A, X, and Y groups excludes the selection of any possible Z group. Accordingly, the Applicants submit that the Z groups listed in Claim 65 were described in the specification as filed and do not constitute new matter.

The Official Action also asserts that the recitation of "Y is $=SO_3H$" in Claim 65 is new matter because the specification teaches a single bond, but not a double bond. Claim 65 has been amended in accordance with the Examiner's helpful suggestion. Accordingly, the reconsideration and withdrawal of the rejection over enablement is respectfully requested.

In light of the foregoing Remarks, the Applicants respectfully submit that the Application is in condition for allowance. A Notice to that effect is respectfully requested.

Respectfully submitted,

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